REMARKS

Claims 1 to 55 are pending. Claims 7, 8, 23, 24, and 35 to 55 have been withdrawn from consideration. Claims 4 to 6 are canceled. Claim 56 is added. Thus, claims 1 to 3, 9 to 22, 25 to 34, and 56 are under consideration.

Claims 1 to 3, 9, 25, and 34 are amended.

Amendments to the specification

The specification has been amended to correct a typographical error and to provide updated citations to patent applications.

The typographical error occurred in the citation of International Patent Publication No. WO 02/085905, cited as a reference describing certain adenine derivatives. The typographical error results in citation of a published application to a method and device for controlling a drive unit, which bears no relation to adenine derivatives or any other aspect of Applicants' disclosure.

No new matter is introduced by these amendments.

Amendments to the claims

Claim 1 has been amended to recite a method of identifying a compound that selectively modulates TLR7-mediated cellular activity vs. TLR8-mediated cellular activity. Further, the assays to detect modulation of a TLR-mediated cellular activity are performed using a test compound and human cells that naturally express TLR7 and/or TLR8. The amendment is supported throughout Applicants' disclosure at, for example, page 9, lines 17-23; page 22, lines 20-30; Examples 3 and 4 (pages 39-41); and original claims 4 and 5.

Claim 2 is amended to recite that the test compound modulates a TLR7-mediated cellular activity and does not modulate a TLR8-mediated cellular activity. This amendment is fully supported throughout Applicants' disclosure at, for example, page 7, lines 4-27.

Claim 3 is amended to recite that the test compound modulates a TLR8-mediated cellular activity and does not modulate a TLR7-mediated cellular activity. This amendment is fully supported throughout Applicants' disclosure at, for example, page 7, lines 4-27.

Claim 9 is amended to correct formalities.

Claim 25 is amended to correct formalities and to recite a method of selectively modulating TLR7-mediated cellular activity vs. TLR8-mediated cellular activity of in human immune cells that naturally express TLR7 and/or TLR8. The amendment is fully supported throughout the application at, for example, page 9, lines 17-23; page 22, lines 20-30; and Examples 3 and 4 (pages 39-41).

Claim 34 is amended to correct a typographical error.

New claim 56 recites the method of claim 25 wherein the compound modulates TLR8-mediated cellular activity and does not detectably modulate TLR7-mediated cellular activity. This amendment is patentable as it depends from independent claim 25, which is patentable for reasons set forth in detail below. Claim 56 is fully supported by Applicants' disclosure at, for example, page 7, lines 4-21.

No new matter is introduced by these amendments.

§ 112 Rejections

Claims 1 to 6, 9 to 22, and 25 to 34 stand rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Specifically, claims 1, 9, and 25 (the independent claims) are rejected as being incomplete for omitting essential steps. Claims 1 is asserted to omit steps of identifying which assay to use, starting material for the method, what to test for, and what result to expect. Claim 9 is asserted to omit to how to identify a TLR modulation profile. Claim 25 is asserted to omit how to identify cell populations for the method, what characteristics to look for in the cell populations, and what differences or similarities to expect. Applicants' respectfully traverse the rejection.

The asserted deficiencies in claim 1 are all related—the starting material, the endpoint of the assay, and the expected result all depend upon the particular assay chosen in the practice of the invention. Applicants submit that the claims are clear and definite to those skilled in the art armed with the teaching in Applicants' disclosure and having knowledge of available assays for detecting cellular activities.

Applicants provide detailed description of one such assay at, for example, page 22, lines 20-30. Myeloid dendritic cells (mDCs) are activated by a TLR7/8 agonist and a TLR8-selective

agonist, but are not activated by a TLR7-selective agonist. Plasmacytoid dendritic cells (pDCs), on the other hand, are activated by a TLR7/8 agonist and a TLR7-selective agonist, but not a TLR8-selective agonist. Therefore, the selectivity of a test compound with respect to TLR7 and TLR8 can be determined by contacting the test compound with a population of mDCs and a separate population of pDCs. A test compound that activates mDCs but not pDCs is TLR8-selective; a test compound that activates pDCs but not mDCs is TLR7-selective.

Applicants' disclosure, therefore, describes the assay to be used (activation of mDCs and pDCs), the starting material (mDCs, pDCs, and test compound), what to test for (CD80 expression by each population of cells), and what result to expect (test compound will activate one cell population and not the other).

Those skilled in the art, armed with Applicants' disclosure and having knowledge of the expression of various TLRs among populations of immune cells, can (a) modify the assay described in Applicants' disclosure to use detect TLR-selectivity of a test compound, or (b) employ other assays known to detect TLR function.

Applicants submit that claim 1 is definite and therefore satisfies the requirements of 35 U.S.C. § 112, second paragraph. Claims 2 and 3 stand rejected as depending from claim 1. Absent some additional deficiency, Applicants submit that claims 2 and 3 also satisfy the requirements of U.S.C. § 112, second paragraph.

The asserted deficiencies of claim 9 are similar to those enumerated for claim 1—i.e., starting materials, type of assay, and expected results. Applicants therefore submit that that those skilled in the art, armed with Applicants' disclosure and having knowledge of the expression of various TLRs among populations of immune cells, can practice the method recited in claim 9.

Additionally, the Office Action asserts that no meaningful interpretation can be obtained for claims 9 to 24, because "the disclosure does not describe or teach how to identify a 'TLR modulation profile'." Applicants respectfully disagree. Applicants' disclosure defines a "TLR modulation profile" at page 6, lines 7-16. Included in that definition is the following:

> The TLR modulation profile of a given compound refers to the observed profile of TLR-mediated cellular activities modulated by the given compound. The observed profile may be compiled from a single source or multiple sources and may be derived from, for

example, experimental assay results, clinical or anecdotal observations, or any other suitable source.

Thus, one skilled in the art can identify the TLR modulation profile for any specific compound from the known TLR agonist properties of the compound, collected from any of the enumerated sources. That is, one skilled in the art can identify whether a compound is, for example, a TLR7 agonist, a TLR7/8 agonist, a TLR7-selective agonist, a TLR2/6 agonist, a TLR8 agonist, a TLR8-selective agonist, a TLR9 agonist, etc. Applicants provide further detail and examples of particular considerations that may go into a TLR modulation profile for any particular application. See, e.g., page 17, line 13 through page 20 line 19, especially, for example, page 17, lines 22-25; page 18, lines 11-14; page 19, lines 10-18; and page 20, lines 3-19.

Applicants submit that claim 9 is definite and therefore satisfies the requirements of 35 U.S.C. § 112, second paragraph. Claims 10 to 22 stand rejected as depending, directly or indirectly, from claim 9. Absent some additional deficiency, Applicants submit that claims 10 to 22 also satisfy the requirements of U.S.C. § 112, second paragraph.

With respect to claim 25, the Office Action asserts that neither the claim nor the specification describes how to select the first and second immune cell populations, what characteristics to look for in each cell population and what differences or similarities to expect. Applicants respectfully disagree.

The claim recites a method for selectively modulating cells of the immune system. One skilled in the art, seeking to practice the invention, would approach the method with the starting cell populations in mind, for why else would that person want to selectively modulate the activity of the cells?

One characteristic that a person skilled in the art can look for is TLR expression profile. TLR expression profiles of some representative immune cells populations are summarized in Applicants' disclosure (see, e.g., page 21, lines 15-26).

Finally, the claim specifically recites that the selected compound modulates a TLR-mediated cellular activity of the first cell population to a different extent than it modulates a TLR-mediated cellular activity of the second cell population. Applicants' disclosure identifies

suitable cellular activities at, for example, page 10, lines 3-10. The particular cellular activity will be determined by the cell populations between which selective modulation is desired.

Applicants submit that claim 25 is definite and therefore satisfies the requirements of 35 U.S.C. § 112, second paragraph. Claims 26 to 34 stand rejected as depending, directly or indirectly, from claim 25. Absent some additional deficiency, Applicants submit that claims 26 to 34 also satisfy the requirements of U.S.C. § 112, second paragraph.

In summary, Applicants submit that 1 to 3, 9 to 22, 25 to 34 satisfy the requirements of 35 USC § 112, second paragraph, and request that the rejection be withdrawn.

§ 102 Rejections

Claims 1 to 6 and 25 to 34 stand rejected under 35 USC § 102(b) as being anticipated by Hemmi *et al.* Claims 1 and 25 have been amended herein.

Claim 1 has been amended to recite that each assay is performed using the test compound and human cells that naturally express TLR7 and/or TLR8. Hemmi *et al.* teaches only the use of the murine cells. This is a non-trivial distinction. Among the many differences between murine immunity and human immunity is that while human immune cells such as, for example, mDCs, possess functional TLR8, murine immune cells lack a functional TLR8.

Consequently, claim 1 is novel over Hemmi *et al.* Each of claims 2 and 3 depends from claim 1 and is, therefore, is novel over Hemmi *et al.* for at least all of the reasons provided regarding the novelty of claim 1.

Claim 25 has been amended to recite a method of selectively modulating TLR7-mediated cellular activity vs. TLR8-mediated cellular activity of two human immune cell populations that naturally express TLR7 and TLR8, respectively. The teachings of Hemmi *et al.* are limited to (a) murine cells, and (b) artificial cellular construct based on human kidney cells (HEK293 cells) that neither naturally express TLRs nor generate natural TLR-mediated cellular activities.

Consequently, claim 25 is novel over Hemmi *et al.* Each of claims 26 to 34 depends, directly or indirectly, from claim 25 and is, therefore, is novel over Hemmi *et al.* for at least all of the reasons provided regarding the novelty of claim 25.

Applicants submit that claims 1 to 3 and 25 to 34 are novel over Hemmi *et al.* and request that the rejection of those claims under 35 USC § 102(b) be withdrawn.

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Claims 1 to 6 stand rejected under 35 USC § 102(a) as being anticipated by Jurk *et al.* Claim 1 has been amended to recite that each assay is performed using the test compound and human cells that naturally express TLR7 and/or TLR8. Jurk *et al.* teaches only the activation of an artificial cellular construct based on human kidney cells. The artificial constructs neither naturally express TLRs nor generate natural TLR-mediated cellular activities.

Applicants submit that claims 1 to 3 are novel over Jurk *et al.* and request that the rejection of those claims under 35 USC § 102(a) be withdrawn.

Claims 1 to 6 stand rejected under 35 USC § 102(a) as being anticipated by Gibson *et al.* (*Cellular Immunology*, vol. 218 (2002), pp. 74-86). Claim 1 has been amended to recite identification of compounds that selectively modify TLR7-mediated cellular activity vs. TLR8-mediated cellular activity. Gibson *et al.* fails to teach selective modulation of TLR7-mediated cellular activity vs. TLR8-mediated cellular activity.

Applicants submit that claims 1 to 3 are novel over Gibson *et al.* and request that the rejection of those claims under 35 USC § 102(a) be withdrawn.

CONCLUSION

In view of the above, it is submitted that the application is in condition for allowance. Reconsideration of the application is requested.

Allowance of claims 1 to 3, 9 to 22, 25 to 34, and 56 at an early date is solicited.

Respectfully submitted,

1/29/2007
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